SEQUENCE LISTING

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 Felipe A. Andrade
 Sophie Roy
 Nancy A. Thornberry

<120> AUTOANTIGENIC FRAGMENTS, METHODS AND ASSAYS

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AUG 0 I 2003

TECH CENTER 1600/2900

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Cys Ser Ile Phe Ile Lys Ile Ile Asp Arg Ile His Gly Thr Glu Glu
                           40
                                                45
Gly Gln Gln Ile Leu Lys Gln Pro Val Ser Glu Arg Leu Asp Phe Val
                       55
                                           60
Cys Ser Phe Leu Gln Lys Asn Arg Lys His Pro Ser Ser Pro Glu Cys
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Leu Val Ser Ala Gln Lys Val Leu Glu Gly Ser Glu Leu Glu Leu Ala
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Lys Met Thr Met Leu Leu Tyr His Ser Thr Met Ser Ser Lys Ser Pro Arg Asp Trp Glu Gln Phe Glu Tyr Lys Ile Gln Ala Glu Leu Ala Val Ile Leu Lys Phe Val Leu Asp His Glu Asp Gly Leu Asn Leu Asn Glu Asp Leu Glu Asn Phe Leu Gln Lys Ala Pro Val Pro Ser Thr Cys Ser Ser Thr Phe Pro Glu Glu Leu Ser Pro Pro Ser His Gln Ala Lys Arg Glu Ile Arg Phe Leu Glu Leu Gln Lys Val Ala Ser Ser Ser Ser Gly Asn Asn Phe Leu Ser Gly Ser Pro Ala Ser Pro Met Gly Asp Ile Leu Gln Thr Pro Gln Phe Gln Met Arg Arg Leu Lys Lys Gln Leu Ala Asp Glu Arg Ser Asn Arg Asp Glu Leu Glu Leu Glu Leu Ala Glu Asn Arg Lys Leu Leu Thr Glu Lys Asp Ala Gln Ile Ala Met Met Gln Gln Arg Ile Asp Arg Leu Ala Leu Leu Asn Glu Lys Gln Ala Ala Ser Pro Leu Glu Pro Lys Glu Leu Glu Glu Leu Arg Asp Lys Asn Glu Ser Leu Thr Met Arg Leu His Glu Thr Leu Lys Gln Cys Gln Asp Leu Lys Thr Glu Lys Ser Gln Met Asp Arg Lys Ile Asn Gln Leu Ser Glu Glu Asn Gly Asp Leu Ser Phe Lys Leu Arg Glu Phe Ala Ser His Leu Gln Gln Leu Gln Asp Ala Leu Asn Glu Leu Thr Glu Glu His Ser Lys Ala Thr Gln Glu Trp Leu Glu Lys Gln Ala Gln Leu Glu Lys Glu Leu Ser Ala Ala Leu Gln Asp Lys Lys Cys Leu Glu Glu Lys Asn Glu Ile Leu Gln Gly Lys Leu Ser Gln Leu Glu Glu His Leu Ser Gln Leu Gln Asp Asn Pro Pro Gln Glu Lys Gly Glu Val Leu Gly Asp Val Leu Gln Leu Glu Thr Leu Lys Gln Glu Ala Ala Thr Leu Ala Ala Asn Asn Thr Gln Leu Gln Ala Arg Val Glu Met Leu Glu Thr Glu Arg Gly Gln Gln Glu Ala Lys Leu Leu Ala Glu Arg Gly His Phe Glu Glu Glu Lys Gln Gln Leu Ser Ser Leu Ile Thr Asp Leu Gln Ser Ser Ile Ser Asn Leu Ser Gln Ala Lys Glu Glu Leu Glu Gln Ala Ser Gln Ala His Gly Ala Arg Leu Thr Ala Gln Val Ala Ser Leu Thr Ser Glu Leu Thr Thr Leu Asn Ala Thr Ile Gln Gln Gln Asp Gln Glu Leu Ala Gly Leu Lys Gln Gln Ala

Lys Glu Lys Gln Ala Gln Leu Ala Gln Thr Leu Gln Gln Gln Gln Ala Ser Gln Gly Leu Arg His Gln Val Glu Gln Leu Ser Ser Leu Lys Gln Lys Glu Gln Gln Leu Lys Glu Val Ala Glu Lys Gln Glu Ala Thr Arg Gln Asp His Ala Gln Gln Leu Ala Thr Ala Ala Glu Glu Arg Glu Ala Ser Leu Arg Glu Arg Asp Ala Ala Leu Lys Gln Leu Glu Ala Leu Glu Lys Glu Lys Ala Ala Lys Leu Glu Ile Leu Gln Gln Gln Leu Gln Val Ala Asn Glu Ala Arg Asp Ser Ala Gln Thr Ser Val Thr Gln Ala Gln Arg Glu Lys Ala Glu Leu Ser Arg Lys Val Glu Glu Leu Gln Ala Cys Val Glu Thr Ala Arg Gln Glu Gln His Glu Ala Gln Ala Gln Val Ala Glu Leu Glu Leu Gln Leu Arg Ser Glu Gln Gln Lys Ala Thr Glu Lys Glu Arg Val Ala Gln Glu Lys Asp Gln Leu Gln Glu Gln Leu Gln Ala Leu Lys Glu Ser Leu Lys Val Thr Lys Gly Ser Leu Glu Glu Glu Lys Arg Arg Ala Ala Asp Ala Leu Glu Glu Gln Gln Arg Cys Ile Ser Glu Leu Lys Ala Glu Thr Arg Ser Leu Val Glu Gln His Lys Arg Glu Arg Lys Glu Leu Glu Glu Glu Arg Ala Gly Arg Lys Gly Leu Glu Ala Arg Leu Leu Gln Leu Gly Glu Ala His Gln Ala Glu Thr Glu Val Leu Arg Arg Glu Leu Ala Glu Ala Met Ala Ala Gln His Thr Ala Glu Ser Glu Cys Glu Gln Leu Val Lys Glu Val Ala Ala Trp Arg Asp Gly Tyr Glu Asp Ser Gln Gln Glu Glu Ala Gln Tyr Gly Ala Met Phe Gln Glu Gln Leu Met Thr Leu Lys Glu Glu Cys Glu Lys Ala Arg Gln Glu Leu Gln Glu Ala Lys Glu Lys Val Ala Gly Ile Glu Ser His Ser Glu Leu Gln Ile Ser Arg Gln Gln Asn Lys Leu Ala Glu Leu His Ala Asn Leu Ala Arg Ala Leu Gln Gln Val Gln Glu Lys Glu Val Arg Ala Gln Lys Leu Ala Asp Asp Leu Ser Thr Leu Gln Glu Lys Met Ala Ala Thr Ser Lys Glu Val Ala Arg Leu Glu Thr Leu Val Arg Lys Ala Gly Glu Gln Gln Glu Thr Ala Ser Arg Glu Leu Val Lys Glu Pro Ala Arg Ala Gly Asp Arg Gln Pro Glu Trp Leu Glu Glu Gln Gln Gly Arg Gln Phe

Cys Ser Thr Gln Ala Ala Leu Gln Ala Met Glu Arg Glu Ala Glu Gln Met Gly Asn Glu Leu Glu Arg Leu Arg Ala Ala Leu Met Glu Ser Gln Gly Gln Gln Glu Glu Arg Gly Gln Gln Glu Arg Glu Val Ala Arg Leu Thr Gln Glu Arg Gly Arg Ala Gln Ala Asp Leu Ala Leu Glu Lys Ala Ala Arg Ala Glu Leu Glu Met Arg Leu Gln Asn Ala Leu Asn Glu Gln Arg Val Glu Phe Ala Thr Leu Gln Glu Ala Leu Ala His Ala Leu Thr Glu Lys Glu Gly Lys Asp Gln Glu Leu Ala Lys Leu Arg Gly Leu Glu Ala Ala Gln Ile Lys Glu Leu Glu Glu Leu Arg Gln Thr Val Lys Gln Leu Lys Glu Gln Leu Ala Lys Lys Glu Lys Glu His Ala Ser Gly Ser Gly Ala Gln Ser Glu Ala Ala Gly Arg Thr Glu Pro Thr Gly Pro Lys Leu Glu Ala Leu Arg Ala Glu Val Ser Lys Leu Glu Gln Gln Cys Gln Lys Gln Gln Glu Gln Ala Asp Ser Leu Glu Arg Ser Leu Glu Ala 1140 1145 Glu Arg Ala Ser Arg Ala Glu Arg Asp Ser Ala Leu Glu Thr Leu Gln 1160 1165 Gly Gln Leu Glu Glu Lys Ala Gln Glu Leu Gly His Ser Gln Ser Ala Leu Ala Ser Ala Gln Arg Glu Leu Ala Ala Phe Arg Thr Lys Val Gln Asp His Ser Lys Ala Glu Asp Glu Trp Lys Ala Gln Val Ala Arg Gly Arg Gln Glu Ala Glu Arg Lys Asn Ser Leu Ile Ser Ser Leu Glu Glu Glu Val Ser Ile Leu Asn Arg Gln Val Leu Glu Lys Glu Gly Glu Ser Lys Glu Leu Lys Arg Leu Val Met Ala Glu Ser Glu Lys Ser Gln Lys Leu Glu Glu Ser Cys Ala Cys Cys Arg Gln Arg Gln Pro Ala Thr Val Pro Glu Leu Gln Asn Ala Ala Leu Leu Cys Gly Arg Arg Cys Arg Ala Ser Gly Arg Glu Ala Glu Lys Gln Arg Val Ala Ser Glu Asn Leu Arg Gln Glu Leu Thr Ser Gln Ala Glu Arg Ala Glu Glu Leu Gly Gln Glu Leu Lys Ala Trp Gln Glu Lys Phe Phe Gln Lys Glu Gln Ala Leu Ser Thr Leu Gln Leu Glu His Thr Ser Thr Gln Ala Leu Val Ser Glu Leu Leu Pro Ala Lys His Leu Cys Gln Gln Leu Gln Ala Glu Gln Ala Ala Ala Glu Lys Arg His Arg Glu Glu Leu Glu Gln Ser Lys Gln Ala Ala

Gly Gly Leu Arg Ala Glu Leu Leu Arg Ala Gln Arg Glu Leu Gly Glu Leu Ile Pro Leu Arg Gln Lys Val Ala Glu Gln Glu Arg Thr Ala Gln Gln Leu Arg Ala Glu Lys Ala Ser Tyr Ala Glu Gln Leu Ser Met Leu Lys Lys Ala His Gly Leu Leu Ala Glu Glu Asn Arg Gly Leu Gly Glu Arg Ala Asn Leu Gly Arg Gln Phe Leu Glu Val Glu Leu Asp Gln Ala Arg Glu Lys Tyr Val Gln Glu Leu Ala Ala Val Arg Ala Asp Ala Glu Thr Arg Leu Ala Glu Val Gln Arg Glu Ala Gln Ser Thr Ala Arg Glu Leu Glu Val Met Thr Ala Lys Tyr Glu Gly Ala Lys Val Lys Val Leu Glu Glu Arg Gln Arg Phe Gln Glu Glu Arg Gln Lys Leu Thr Ala Gln Val Glu Glu Leu Ser Lys Lys Leu Ala Asp Ser Asp Gln Ala Ser Lys 1540 1545 Val Gln Gln Gln Lys Leu Lys Ala Val Gln Ala Gln Gly Gly Glu Ser 1555 1560 Gln Gln Glu Ala Gln Arg Phe Gln Ala Gln Leu Asn Glu Leu Gln Ala Gln Leu Ser Gln Lys Glu Gln Ala Ala Glu His Tyr Lys Leu Gln Met 1590 1595 Glu Lys Ala Lys Thr His Tyr Asp Ala Lys Lys Gln Gln Asn Gln Glu Leu Gln Glu Gln Leu Arg Ser Leu Glu Gln Leu Gln Lys Glu Asn Lys Glu Leu Arg Ala Glu Ala Glu Arg Leu Gly His Glu Leu Gln Gln Ala Gly Leu Lys Thr Lys Glu Ala Glu Gln Thr Cys Arg His Leu Thr Ala Gln Val Arg Ser Leu Glu Ala Gln Val Ala His Ala Asp Gln Gln Leu Arg Asp Leu Gly Lys Phe Gln Val Ala Thr Asp Ala Leu Lys Ser Arg 1685 1690 Glu Pro Gln Ala Lys Pro Gln Leu Asp Leu Ser Ile Asp Ser Leu Asp Leu Ser Cys Glu Glu Gly Thr Pro Leu Ser Ile Thr Ser Lys Leu Pro 1715 1720 Arg Thr Gln Pro Asp Gly Thr Ser Val Pro Gly Glu Pro Ala Ser Pro Ile Ser Gln Arg Leu Pro Pro Lys Val Glu Ser Leu Glu Ser Leu Tyr Phe Thr Pro Ile Pro Ala Arg Ser Gln Ala Pro Leu Glu Ser Ser Leu Asp Ser Leu Gly Asp Val Phe Leu Asp Ser Gly Arg Lys Thr Arg Ser Ala Arg Arg Arg Thr Thr Gln Ile Ile Asn Ile Thr Met Thr Lys Lys Leu Asp Val Glu Glu Pro Asp Ser Ala Asn Ser Ser Phe Tyr Ser Thr

Arg Ser Ala Pro Ala Ser Gln Ala Ser Leu Arg Ala Thr Ser Ser Thr 1830 1835 Gln Ser Leu Ala Arg Leu Gly Ser Pro Asp Tyr Gly Asn Ser Ala Leu 1845 1850 Leu Ser Leu Pro Gly Tyr Arg Pro Thr Thr Arg Ser Ser Ala Arg Arg 1860 1865 1870 Ser Gln Ala Gly Val Ser Ser Gly Ala Pro Pro Gly Arg Asn Ser Phe 1875 1880 1885 Tyr Met Gly Thr Cys Gln Asp Glu Pro Glu Gln Leu Asp Asp Trp Asn 1895 1900 Arg Ile Ala Glu Leu Gln Gln Arg Asn Arg Val Cys Pro Pro His Leu 1910 1915 Lys Thr Cys Tyr Pro Leu Glu Ser Arg Pro Ser Leu Ser Leu Gly Thr 1925 1930 Ile Thr Asp Glu Glu Met Lys Thr Gly Asp Pro Gln Glu Thr Leu Arg 1940 1945 1950 Arg Ala Ser Met Gln Pro Ile Gln Ile Ala Glu Gly Thr Gly Ile Thr 1955 1960 1965 Thr Arg Gln Gln Arg Lys Arg Val Ser Leu Glu Pro His Gln Gly Pro 1975 1980 Gly Thr Pro Glu Ser Lys Lys Ala Thr Ser Cys Phe Pro Arg Pro Met 1985 1990 1995 2000 Thr Pro Arg Asp Arg His Glu Gly Arg Lys Gln Ser Thr Thr Glu Ala 2005 2010 Gln Lys Lys Ala Ala Pro Ala Ser Thr Lys Gln Ala Asp Arg Arg Gln 2020 2030 2025 Ser Met Ala Phe Ser Ile Leu Asn Thr Pro Lys Lys Leu Gly Asn Ser 2040 2045 Leu Leu Arg Arg Gly Ala Ser Lys Lys Ala Leu Ser Lys Ala Ser Pro 2055 2060 Asn Thr Arg Ser Gly Thr Arg Arg Ser Pro Arg Ile Ala Thr Thr 2070 2075 Ala Ser Ala Ala Thr Ala Ala Ala Ile Gly Ala Thr Pro Arg Ala Lys 2085 2090 Gly Lys Ala Lys His 2100

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Ser Leu His Val Ala Asp Pro Val Glu Ala Val Leu Gln Leu Gln Asp
20
25
30

Cys Ser Ile Phe Ile Lys Ile Ile Asp Arg Ile His Gly Thr Glu Glu
35 40 45

Gly Gln Gln Ile Leu Lys Gln Pro Val Ser Glu Arg Leu Asp Phe Val
50 55 60

Cys Ser Phe Leu Gln Lys Asn Arg Lys His Pro Ser Ser Pro Glu Cys 70 75 80

Leu Val Ser Ala Gln Lys Val Leu Glu Gly Ser Glu Leu Glu Leu Ala Lys Met Thr Met Leu Leu Tyr His Ser Thr Met Ser Ser Lys Ser Pro Arg Asp Trp Glu Gln Phe Glu Tyr Lys Ile Gln Ala Glu Leu Ala Val Ile Leu Lys Phe Val Leu Asp His Glu Asp Gly Leu Asn Leu Asn Glu Asp Leu Glu Asn Phe Leu Gln Lys Ala Pro Val Pro Ser Thr Cys Ser Ser Thr Phe Pro Glu Glu Leu Ser Pro Pro Ser His Gln Ala Lys Arg Glu Ile Arg Phe Leu Glu Leu Gln Lys Val Ala Ser Ser Ser Gly Asn Asn Phe Leu Ser Gly Ser Pro Ala Ser Pro Met Gly Asp Ile Leu Gln Thr Pro Gln Phe Gln Met Arg Arg Leu Lys Lys Gln Leu Ala Asp Glu Arg Ser Asn Arg Asp Glu Leu Glu Leu Glu Leu Ala Glu Asn Arg Lys Leu Leu Thr Glu Lys Asp Ala Gln Ile Ala Met Met Gln Gln Arg Ile Asp Arg Leu Ala Leu Leu Asn Glu Lys Gln Ala Ala Ser Pro Leu Glu Pro Lys Glu Leu Glu Glu Leu Arg Asp Lys Asn Glu Ser Leu Thr Met Arg Leu His Glu Thr Leu Lys Gln Cys Gln Asp Leu Lys Thr Glu Lys Ser Gln Met Asp Arg Lys Ile Asn Gln Leu Ser Glu Glu Asn Gly Asp Leu Ser Phe Lys Leu Arg Glu Phe Ala Ser His Leu Gln Gln Leu Gln Asp Ala Leu Asn Glu Leu Thr Glu Glu His Ser Lys Ala Thr Gln Glu Trp Leu Glu Lys Gln Ala Gln Leu Glu Lys Glu Leu Ser Ala Ala Leu Gln Asp Lys Lys Cys Leu Glu Glu Lys Asn Glu Ile Leu Gln Gly Lys Leu Ser Gln Leu Glu Glu His Leu Ser Gln Leu Gln Asp Asn Pro Pro Gln Glu Lys Gly Glu Val Leu Gly Asp Val Leu Gln Leu Glu Thr Leu Lys Gln Glu Ala Ala Thr Leu Ala Ala Asn Asn Thr Gln Leu Gln Ala Arg Val Glu Met Leu Glu Thr Glu Arg Gly Gln Gln Glu Ala Lys Leu Leu Ala Glu Arg Gly His Phe Glu Glu Glu Lys Gln Gln Leu Ser Ser Leu Ile Thr Asp Leu Gln Ser Ser Ile Ser Asn Leu Ser Gln Ala Lys Glu Glu Leu Glu Gln Ala Ser Gln Ala His Gly Ala Arg Leu Thr Ala Gln Val Ala Ser Leu Thr Ser Glu Leu Thr Thr Leu Asn Ala

Thr Ile Gln Gln Asp Gln Glu Leu Ala Gly Leu Lys Gln Gln Ala Lys Glu Lys Gln Ala Gln Leu Ala Gln Thr Leu Gln Gln Glu Gln Ala Ser Gln Gly Leu Arg His Gln Val Glu Gln Leu Ser Ser Leu Lys Gln Lys Glu Gln Gln Leu Lys Glu Val Ala Glu Lys Gln Glu Ala Thr Arg Gln Asp His Ala Gln Gln Leu Ala Thr Ala Ala Glu Glu Arg Glu Ala Ser Leu Arg Glu Arg Asp Ala Ala Leu Lys Gln Leu Glu Ala Leu Glu Lys Glu Lys Ala Ala Lys Leu Glu Ile Leu Gln Gln Gln Leu Gln Val Ala Asn Glu Ala Arg Asp Ser Ala Gln Thr Ser Val Thr Gln Ala Gln Arg Glu Lys Ala Glu Leu Ser Arg Lys Val Glu Glu Leu Gln Ala Cys Val Glu Thr Ala Arg Gln Glu Gln His Glu Ala Gln Ala Gln Val Ala Glu Leu Glu Leu Gln Leu Arg Ser Glu Gln Gln Lys Ala Thr Glu Lys Glu Arg Val Ala Gln Glu Lys Asp Gln Leu Gln Glu Gln Leu Gln Ala Leu Lys Glu Ser Leu Lys Val Thr Lys Gly Ser Leu Glu Glu 710 715 Glu Lys Arg Arg Ala Ala Asp Ala Leu Glu Glu Gln Gln Arg Cys Ile Ser Glu Leu Lys Ala Glu Thr Arg Ser Leu Val Glu Gln His Lys Arg Glu Arg Lys Glu Leu Glu Glu Glu Arg Ala Gly Arg Lys Gly Leu Glu Ala Arg Leu Gln Gln Leu Gly Glu Ala His Gln Ala Glu Thr Glu Val Leu Arg Arg Glu Leu Ala Glu Ala Met Ala Ala Gln His Thr Ala Glu Ser Glu Cys Glu Gln Leu Val Lys Glu Val Ala Ala Trp Arg Glu Arg Tyr Glu Asp Ser Gln Gln Glu Glu Ala Gln Tyr Gly Ala Met Phe Gln Glu Gln Leu Met Thr Leu Lys Glu Glu Cys Glu Lys Ala Arg Gln Glu Leu Gln Glu Ala Lys Glu Lys Val Ala Gly Ile Glu Ser His Ser Glu Leu Gln Ile Ser Arg Gln Gln Asn Glu Leu Ala Glu Leu His Ala Asn Leu Ala Arg Ala Leu Gln Gln Val Gln Glu Lys Glu Val Arg Ala Gln Lys Leu Ala Asp Asp Leu Ser Thr Leu Gln Glu Lys Met Ala Ala Thr Ser Lys Glu Val Ala Arg Leu Glu Thr Leu Val Arg Lys Ala Gly Glu Gln Gln Glu Thr Ala Ser Arg Glu Leu Val Lys Glu Pro Ala Arg Ala

Gly Asp Arg Gln Pro Glu Trp Leu Glu Glu Gln Gln Gly Arg Gln Phe Cys Ser Thr Gln Ala Ala Leu Gln Ala Met Glu Arg Glu Ala Glu Gln Met Gly Asn Glu Leu Glu Arg Leu Arg Ala Ala Leu Met Glu Ser Gln Gly Gln Gln Glu Glu Arg Gly Gln Glu Arg Glu Val Ala Arg Leu Thr Gln Glu Arg Gly Arg Ala Gln Ala Asp Leu Ala Leu Glu Lys Ala Ala Arg Ala Glu Leu Glu Met Arg Leu Gln Asn Ala Leu Asn Glu Gln Arg Val Glu Phe Ala Thr Leu Gln Glu Ala Leu Ala His Ala Leu Thr Glu Lys Glu Gly Lys Asp Gln Glu Leu Ala Lys Leu Arg Gly Leu Glu Ala Ala Gln Ile Lys Glu Leu Glu Glu Leu Arg Gln Thr Val Lys Gln Leu Lys Glu Gln Leu Ala Lys Lys Glu Lys Glu His Ala Ser Gly 1090 1095 Ser Gly Ala Gln Ser Glu Ala Ala Gly Arg Thr Glu Pro Thr Gly Pro 1110 1115 Lys Leu Glu Ala Leu Arg Ala Glu Val Ser Lys Leu Glu Gln Gln Cys Gln Lys Gln Gln Glu Gln Ala Asp Ser Leu Glu Arg Ser Leu Glu Ala 1140 1145 1150 Glu Arg Ala Ser Arg Ala Glu Arg Asp Ser Ala Leu Glu Thr Leu Gln Gly Gln Leu Glu Glu Lys Ala Gln Glu Leu Gly His Ser Gln Ser Ala 1170 1175 Leu Ala Ser Ala Gln Arg Glu Leu Ala Ala Phe Arg Thr Lys Val Gln Asp His Ser Lys Ala Glu Asp Glu Trp Lys Ala Gln Val Ala Arg Gly Arg Gln Glu Ala Glu Arg Lys Asn Ser Leu Ile Ser Ser Leu Glu Glu Glu Val Ser Ile Leu Asn Arg Gln Val Leu Glu Lys Glu Gly Glu Ser Lys Glu Leu Lys Arg Leu Val Met Ala Glu Ser Glu Lys Ser Gln Lys 1250 1255 1260 Leu Glu Glu Arg Leu Arg Leu Leu Gln Ala Glu Thr Ala Ser Asn Ser Ala Arg Ala Ala Glu Arg Ser Ser Ala Leu Arg Glu Glu Val Gln Ser 1285 1290 Leu Arg Glu Glu Ala Glu Lys Gln Arg Val Ala Ser Glu Asn Leu Arg Gln Glu Leu Thr Ser Gln Ala Glu Arg Ala Glu Glu Leu Gly Gln Glu Leu Lys Ala Trp Gln Glu Lys Phe Phe Gln Lys Glu Gln Ala Leu Ser Thr Leu Gln Leu Glu His Thr Ser Thr Gln Ala Leu Val Ser Glu Leu Leu Pro Ala Lys His Leu Cys Gln Gln Leu Gln Ala Glu Gln Ala Ala

Ala Glu Lys Arg His Arg Glu Glu Leu Glu Gln Ser Lys Gln Ala Ala Gly Gly Leu Arg Ala Glu Leu Leu Arg Ala Gln Arg Glu Leu Gly Glu Leu Ile Pro Leu Arg Gln Lys Val Ala Glu Gln Glu Arg Thr Ala Gln Gln Leu Arg Ala Glu Lys Ala Ser Tyr Ala Glu Gln Leu Ser Met Leu Lys Lys Ala His Gly Leu Leu Ala Glu Glu Asn Arg Gly Leu Gly Glu Arg Ala Asn Leu Gly Arg Gln Phe Leu Glu Val Glu Leu Asp Gln Ala 1465 • 1470 Arg Glu Lys Tyr Val Gln Glu Leu Ala Ala Val Arg Ala Asp Ala Glu Thr Arg Leu Ala Glu Val Gln Arg Glu Ala Gln Ser Thr Ala Arg Glu Leu Glu Val Met Thr Ala Lys Tyr Glu Gly Ala Lys Val Lys Val Leu Glu Glu Arg Gln Arg Phe Gln Glu Glu Arg Gln Lys Leu Thr Ala Gln Val Glu Gln Leu Glu Val Phe Gln Arg Glu Gln Thr Lys Gln Val Glu 1540 1545 Glu Leu Ser Lys Lys Leu Ala Asp Ser Asp Gln Ala Ser Lys Val Gln 1555 1560 Gln Gln Lys Leu Lys Ala Val Gln Ala Gln Gly Gly Glu Ser Gln Gln Glu Ala Gln Arg Leu Gln Ala Gln Leu Asn Glu Leu Gln Ala Gln Leu 1590 1595 Ser Gln Lys Glu Gln Ala Ala Glu His Tyr Lys Leu Gln Met Glu Lys Ala Lys Thr His Tyr Asp Ala Lys Lys Gln Gln Asn Gln Glu Leu Gln Glu Gln Leu Arg Ser Leu Glu Gln Leu Gln Lys Glu Asn Lys Glu Leu Arg Ala Glu Ala Glu Arg Leu Gly His Glu Leu Gln Gln Ala Gly Leu Lys Thr Lys Glu Ala Glu Gln Thr Cys Arg His Leu Thr Ala Gln Val Arg Ser Leu Glu Ala Gln Val Ala His Ala Asp Gln Gln Leu Arg Asp Leu Gly Lys Phe Gln Val Ala Thr Asp Ala Leu Lys Ser Arg Glu Pro Gln Ala Lys Pro Gln Leu Asp Leu Ser Ile Asp Ser Leu Asp Leu Ser Cys Glu Glu Gly Thr Pro Leu Ser Ile Thr Ser Lys Leu Pro Arg Thr Gln Pro Asp Gly Thr Ser Val Pro Gly Glu Pro Ala Ser Pro Ile Ser Gln Arg Leu Pro Pro Lys Val Glu Ser Leu Glu Ser Leu Tyr Phe Thr Pro Ile Pro Ala Arg Ser Gln Ala Pro Leu Glu Ser Ser Leu Asp Ser Leu Gly Asp Val Phe Gln Asp Ser Gly Arg Lys Thr Arg Ser Ala Arg . 1805

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Arg Arg Thr Thr Gln Ile Ile Asn Ile Thr Met Thr Lys Lys Leu Asp
                   1815
                                    1820
Val Glu Glu Pro Asp Ser Ala Asn Ser Ser Phe Tyr Ser Thr Arg Ser
               1830
                                1835
Ala Pro Ala Ser Gln Ala Ser Leu Arg Ala Thr Ser Ser Thr Gln Ser
            1845
                                    1855
                             1850
Leu Ala Arg Leu Gly Ser Pro Asp Tyr Gly Asn Ser Ala Leu Leu Ser
          1860
                         1865
                                           1870
Leu Pro Gly Tyr Arg Pro Thr Thr Arg Ser Ser Ala Arg Arg Ser Gln
      1875
                       1880
                                        1885
Ala Gly Val Ser Ser Gly Ala Pro Pro Gly Arg Asn Ser Phe Tyr Met
                   1895
                                    1900
Gly Thr Cys Gln Asp Glu Pro Glu Gln Leu Asp Asp Trp Asn Arg Ile
               1910
                                1915
Ala Glu Leu Gln Gln Arg Asn Arg Val Cys Pro Pro His Leu Lys Thr
            1925
                          1930 1935
Cys Tyr Pro Leu Glu Ser Arg Pro Ser Leu Ser Leu Gly Thr Ile Thr
          1940
                          1945
                                          1950
Asp Glu Glu Met Lys Thr Gly Asp Pro Gln Glu Thr Leu Arg Arg Ala
      1955 1960
                               1965
Ser Met Gln Pro Ile Gln Ile Ala Glu Gly Thr Gly Ile Thr Thr Arg
                   1975 1980
Gln Gln Arg Lys Arg Val Ser Leu Glu Pro His Gln Gly Pro Gly Thr
     1990 1995
Pro Glu Ser Lys Lys Ala Thr Ser Cys Phe Pro Arg Pro Met Thr Pro
             2005
                            2010
Arg Asp Arg His Glu Gly Arg Lys Gln Ser Thr Thr Glu Ala Gln Lys
          2020
                          2025
Lys Ala Ala Pro Ala Ser Thr Lys Gln Ala Asp Arg Arg Gln Ser Met
                      2040
                                       2045
Ala Phe Ser Ile Leu Asn Thr Pro Lys Lys Leu Gly Asn Ser Leu Leu
                   2055
                                    2060
Arg Arg Gly Ala Ser Lys Lys Ala Leu Ser Lys Ala Ser Pro Asn Thr
2065 2070 2075
Arg Ser Gly Thr Arg Arg Ser Pro Arg Ile Ala Thr Thr Ala Ser
            2085
                       2090 2095
Ala Ala Thr Ala Ala Ala Ile Gly Ala Thr Pro Arg Ala Lys Gly Lys
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                          2105
                                           2110
Ala Lys His
      2115
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Met Ala Gly Ser Gly Ala Gly Val Arg Cys Ser Leu Leu Arg Leu Gln

Glu Thr Leu Ser Ala Ala Asp Arg Cys Gly Ala Ala Leu Ala Gly His Gln Leu Ile Arg Gly Leu Gly Gln Glu Cys Val Leu Ser Ser Pro Ala Val Leu Ala Leu Gln Thr Ser Leu Val Phe Ser Arg Asp Phe Gly Leu Leu Val Phe Val Arg Lys Ser Leu Asn Ser Ile Glu Phe Arg Glu Cys Arg Glu Glu Ile Leu Lys Phe Leu Cys Ile Phe Leu Glu Lys Met 8.5 Gly Gln Lys Ile Ala Pro Tyr Ser Val Glu Ile Lys Asn Thr Cys Thr Ser Val Tyr Thr Lys Asp Arg Ala Ala Lys Cys Lys Ile Pro Ala Leu Asp Leu Leu Ile Lys Leu Leu Gln Thr Phe Arg Ser Ser Arg Leu Met Asp Glu Phe Lys Ile Gly Glu Leu Phe Ser Lys Phe Tyr Gly Glu Leu Ala Leu Lys Lys Lys Ile Pro Asp Thr Val Leu Glu Lys Val Tyr Glu Leu Leu Gly Leu Leu Gly Glu Val His Pro Ser Glu Met Ile Asn Asn Ala Glu Asn Leu Phe Arg Ala Phe Leu Gly Glu Leu Lys Thr Gln Met Thr Ser Ala Val Arg Glu Pro Lys Leu Pro Val Leu Ala Gly Cys Leu Lys Gly Leu Ser Ser Leu Leu Cys Asn Phe Thr Lys Ser Met Glu Glu Asp Pro Gln Thr Ser Arg Glu Ile Phe Asn Phe Val Leu Lys Ala Ile Arg Pro Gln Ile Asp Leu Lys Arg Tyr Ala Val Pro Ser Ala Gly Leu Arg Leu Phe Ala Leu His Ala Ser Gln Phe Ser Thr Cys Leu Leu Asp Asn Tyr Val Ser Leu Phe Glu Val Leu Ile Lys Trp Cys Ala His Thr Asn Val Glu Leu Lys Lys Ala Ala Leu Ser Ala Leu Glu Ser Phe Leu Lys Gln Val Ser Asn Met Val Ala Lys Asn Ala Glu Met His Lys Asn Lys Leu Gln Tyr Glu Met Glu Gln Phe Tyr Gly Ile Ile Arg Asn Val Asp Ser Asn Asn Lys Glu Leu Ser Ile Ala Ile Arg Gly Tyr Gly Leu Phe Ala Gly Pro Cys Lys Val Ile Asn Ala Lys Asp Val Asp Phe Met Tyr Val Glu Leu Ile Gln Arg Cys Lys Gln Met Phe Leu Thr Gln Thr Asp Thr Gly Asp Tyr Arg Val Tyr Gln Met Pro Ser Phe Leu Gln Ser Val Ala Ser Val Leu Leu Tyr Leu Asp Thr Val Pro Glu Val Tyr Thr Pro Val Leu Glu His Leu Val Val Met Gln Ile Asp Ser Phe Pro Gln

Tyr Ser Pro Lys Met Gln Leu Val Cys Cys Arg Ala Ile Val Lys Val Phe Leu Ala Leu Ala Ala Lys Gly Pro Val Leu Arg Asn Cys Ile Ser Thr Val Val His Gln Gly Leu Ile Arg Ile Cys Ser Lys Pro Val Val Leu Pro Lys Gly Pro Glu Ser Glu Ser Glu Asp His Arg Ala Ser Gly Glu Val Arg Thr Gly Lys Trp Lys Val Pro Thr Tyr Lys Asp Tyr Val Asp Leu Phe Arg His Leu Leu Ser Ser Asp Gln Met Met Asp Ser Ile Leu Ala Asp Glu Ala Phe Phe Ser Val Asn Ser Ser Ser Glu Ser Leu Asn His Leu Leu Tyr Asp Glu Phe Val Lys Ser Val Leu Lys Ile Val Glu Lys Leu Asp Leu Thr Leu Glu Ile Gln Thr Val Gly Glu Gln Glu Asn Gly Asp Glu Ala Pro Gly Val Trp Met Ile Pro Thr Ser Asp Pro Ala Ala Asn Leu His Pro Ala Lys Pro Lys Asp Phe Ser Ala Phe Ile Asn Leu Val Glu Phe Cys Arg Glu Ile Leu Pro Glu Lys Gln Ala Glu Phe Phe Glu Pro Trp Val Tyr Ser Phe Ser Tyr Glu Leu Ile Leu Gln Ser Thr Arg Leu Pro Leu Ile Ser Gly Phe Tyr Lys Leu Leu Ser Ile Thr Val Arg Asn Ala Lys Lys Ile Lys Tyr Phe Glu Gly Val Ser Pro Lys Ser Leu Lys His Ser Pro Glu Asp Pro Glu Lys Tyr Ser Cys Phe Ala Leu Phe Val Lys Phe Gly Lys Glu Val Ala Val Lys Met Lys Gln Tyr Lys Asp Glu Leu Leu Ala Ser Cys Leu Thr Phe Leu Leu Ser Leu Pro His Asn Ile Ile Glu Leu Asp Val Arg Ala Tyr Val Pro Ala Leu Gln Met Ala Phe Lys Leu Gly Leu Ser Tyr Thr Pro Leu Ala Glu Val Gly Leu Asn Ala Leu Glu Glu Trp Ser Ile Tyr Ile Asp Arg His Val Met Gln Pro Tyr Tyr Lys Asp Ile Leu Pro Cys Leu Asp Gly Tyr Leu Lys Thr Ser Ala Leu Ser Asp Glu Thr Lys Asn Asn Trp Glu Val Ser Ala Leu Ser Arg Ala Ala Gln Lys Gly Phe Asn Lys Val Val Leu Lys His Leu Lys Lys Thr Lys Asn Leu Ser Ser Asn Glu Ala Ile Ser Leu Glu Glu Ile Arg Ile Arg Val Val Gln Met Leu Gly Ser Leu Gly Gly Gln Ile Asn Lys Asn Leu Leu Thr Val Thr Ser Ser Asp Glu Met Met

Lys Ser Tyr Val Ala Trp Asp Arg Glu Lys Arg Leu Ser Phe Ala Val Pro Phe Arg Glu Met Lys Pro Val Ile Phe Leu Asp Val Phe Leu Pro Arg Val Thr Glu Leu Ala Leu Thr Ala Ser Asp Arg Gln Thr Lys Val Ala Ala Cys Glu Leu Leu His Ser Met Val Met Phe Met Leu Gly Lys Ala Thr Gln Met Pro Glu Gly Gly Gln Gly Ala Pro Pro Met Tyr Gln Leu Tyr Lys Arg Thr Phe Pro Val Leu Leu Arg Leu Ala Cys Asp Val Asp Gln Val Thr Arg Gln Leu Tyr Glu Pro Leu Val Met Gln Leu Ile His Trp Phe Thr Asn Asn Lys Lys Phe Glu Ser Gln Asp Thr Val Ser Leu Leu Glu Ala Ile Leu Asp Gly Ile Val Asp Pro Val Asp Ser Thr Leu Arg Asp Phe Cys Gly Arg Cys Ile Arg Glu Phe Leu Lys Trp Ser Ile Lys Gln Ile Thr Pro Gln Gln Glu Lys Ser Pro Val Asn Thr 1045 1050 Lys Ser Leu Phe Lys Arg Leu Tyr Ser Leu Ala Leu His Pro Asn Ala 1060 1065 1070 Phe Lys Arg Leu Gly Ala Ser Leu Ala Phe Asn Asn Ile Tyr Arg Glu 1075 1080 1085 Phe Arg Glu Glu Glu Ser Leu Val Glu Gln Phe Val Phe Glu Ala Leu Val Ile Tyr Met Glu Ser Leu Ala Leu Ala His Ala Asp Glu Lys Ser Leu Gly Thr Ile Gln Gln Cys Cys Asp Ala Ile Asp His Leu Cys Arg Ile Ile Glu Lys Lys His Val Ser Leu Asn Lys Ala Lys Lys Arg Arg Leu Pro Arg Gly Phe Pro Pro Ser Ala Ser Leu Cys Leu Leu Asp Leu Val Lys Trp Leu Leu Ala His Cys Gly Arg Pro Gln Thr Glu Cys Arg His Lys Ser Ile Glu Leu Phe Tyr Lys Phe Val Pro Leu Leu Pro Gly 1185 1190 1195 Asn Arg Ser Pro Asn Leu Trp Leu Lys Asp Val Leu Lys Glu Glu Gly Val Ser Phe Leu Ile Asn Thr Phe Glu Gly Gly Gly Cys Gly Gln Pro Ser Gly Ile Leu Ala Gln Pro Thr Leu Leu Tyr Leu Arg Gly Pro Phe Ser Leu Gln Ala Thr Leu Cys Trp Leu Asp Leu Leu Leu Ala Ala Leu Glu Cys Tyr Asn Thr Phe Ile Gly Glu Arg Thr Val Gly Ala Leu Gln Val Leu Gly Thr Glu Ala Gln Ser Ser Leu Leu Lys Ala Val Ala Phe Phe Leu Glu Ser Ile Ala Met His Asp Ile Ile Ala Ala Glu Lys Cys

Phe Gly Thr Gly Ala Ala Gly Asn Arg Thr Ser Pro Gln Glu Gly Glu 1315 1320 Arg Tyr Asn Tyr Ser Lys Cys Thr Val Val Val Arg Ile Met Glu Phe 1330 1335 1340 Thr Thr Thr Leu Leu Asn Thr Ser Pro Glu Gly Trp Lys Leu Leu Lys 1350 1355 Lys Asp Leu Cys Asn Thr His Leu Met Arg Val Leu Val Gln Thr Leu 1365 1370 Cys Glu Pro Ala Ser Ile Gly Phe Asn Ile Gly Asp Val Gln Val Met 1385 1390 Ala His Leu Pro Asp Val Cys Val Asn Leu Met Lys Ala Leu Lys Met 1395 1400 1405 Ser Pro Tyr Lys Asp Ile Leu Glu Thr His Leu Arg Glu Lys Ile Thr 1415 1420 Ala Gln Ser Ile Glu Glu Leu Cys Ala Val Asn Leu Tyr Gly Pro Asp 1425 1430 1435 Ala Gln Val Asp Arg Ser Arg Leu Ala Ala Val Val Ser Ala Cys Lys 1445 1450 Gln Leu His Arg Ala Gly Leu Leu His Asn Ile Leu Pro Ser Gln Ser 1460 1465 1470 Thr Asp Leu His His Ser Val Gly Thr Glu Leu Leu Ser Leu Val Tyr 1475 1480 Lys Gly Ile Ala Pro Gly Asp Glu Arg Gln Cys Leu Pro Ser Leu Asp 1495 1500 Leu Ser Cys Lys Gln Leu Ala Ser Gly Leu Leu Glu Leu Ala Phe Ala 1510 1515 Phe Gly Gly Leu Cys Glu Arg Leu Val Ser Leu Leu Leu Asn Pro Ala 1525 1530 1535 Val Leu Ser Thr Ala Ser Leu Gly Ser Ser Gln Gly Ser Val Ile His 1540 1545 Phe Ser His Gly Glu Tyr Phe Tyr Ser Leu Phe Ser Glu Thr Ile Asn 1555 1560 1565 Thr Glu Leu Leu Lys Asn Leu Asp Leu Ala Val Leu Glu Leu Met Gln 1575 1580 Ser Ser Val Asp Asn Thr Lys Met Val Ser Ala Val Leu Asn Gly Met 1590 1595 Leu Asp Gln Ser Phe Arg Glu Arg Ala Asn Gln Lys His Gln Gly Leu 1605 1610 1615 Lys Leu Ala Thr Thr Ile Leu Gln His Trp Lys Lys Cys Asp Ser Trp 1620 1625 Trp Ala Lys Asp Ser Pro Leu Glu Thr Lys Met Ala Val Leu Ala Leu 1635 1640 1645 Leu Ala Lys Ile Leu Gln Ile Asp Ser Ser Val Ser Phe Asn Thr Ser 1655 1660 His Gly Ser Phe Pro Glu Val Phe Thr Thr Tyr Ile Ser Leu Leu Ala 1670 1675 Asp Thr Lys Leu Asp Leu His Leu Lys Gly Gln Ala Val Thr Leu Leu 1685 1690 Pro Phe Phe Thr Ser Leu Thr Gly Gly Ser Leu Glu Glu Leu Arg Arg 1700 1705 Val Leu Glu Gln Leu Ile Val Ala His Phe Pro Met Gln Ser Arg Glu 1720 1725 Phe Pro Pro Gly Thr Pro Arg Phe Asn Asn Tyr Val Asp Cys Met Lys 1735 1740

Lys Phe Leu Asp Ala Leu Glu Leu Ser Gln Ser Pro Met Leu Leu Glu 1750 1755 Leu Met Thr Glu Val Leu Cys Arg Glu Gln Gln His Val Met Glu Glu 1770 1775 1765 Leu Phe Gln Ser Ser Phe Arg Arg Ile Ala Arg Arg Gly Ser Cys Val 1780 1785 1790 Thr Gln Val Gly Leu Leu Glu Ser Val Tyr Glu Met Phe Arg Lys Asp 1795 1800 1805 Asp Pro Arg Leu Ser Phe Thr Arg Gln Ser Phe Val Asp Arg Ser Leu 1815 1820 Leu Thr Leu Leu Trp His Cys Ser Leu Asp Ala Leu Arg Glu Phe Phe 1825 1830 1835 Ser Thr Ile Val Val Asp Ala Ile Asp Val Leu Lys Ser Arg Phe Thr 1845 1850 Lys Leu Asn Glu Ser Thr Phe Asp Thr Gln Ile Thr Lys Lys Met Gly 1860 1865 1870 Tyr Tyr Lys Ile Leu Asp Val Met Tyr Ser Arg Leu Pro Lys Asp Asp 1880 1875 1885 Val His Ala Lys Glu Ser Lys Ile Asn Gln Val Phe His Gly Ser Cys 1890 1895 1900 Ile Thr Glu Gly Asn Glu Leu Thr Lys Thr Leu Ile Lys Leu Cys Tyr 1910 1915 Asp Ala Phe Thr Glu Asn Met Ala Gly Glu Asn Gln Leu Leu Glu Arg 1925 1930 1935 Arg Arg Leu Tyr His Cys Ala Ala Tyr Asn Cys Ala Ile Ser Val Ile 1940 1945 1950 Cys Cys Val Phe Asn Glu Leu Lys Phe Tyr Gln Gly Phe Leu Phe Ser 1955 1960 1965 Glu Lys Pro Glu Lys Asn Leu Leu Ile Phe Glu Asn Leu Ile Asp Leu 1970 1975 1980 Lys Arg Arg Tyr Asn Phe Pro Val Glu Val Glu Val Pro Met Glu Arg 1990 1995 2000 Lys Lys Lys Tyr Ile Glu Ile Arg Lys Glu Ala Arg Glu Ala Ala Asn 2005 2010 Gly Asp Ser Asp Gly Pro Ser Tyr Met Ser Ser Leu Ser Tyr Leu Ala 2020 2025 2030 Asp Ser Thr Leu Ser Glu Glu Met Ser Gln Phe Asp Phe Ser Thr Gly 2040 Val Gln Ser Tyr Ser Tyr Ser Ser Gln Asp Pro Arg Pro Ala Thr Gly 2055 Arg Phe Arg Arg Glu Gln Arg Asp Pro Thr Val His Asp Asp Val 2070 2075 Leu Glu Leu Glu Met Asp Glu Leu Asn Arg His Glu Cys Met Ala Pro 2085 2090 2095 Leu Thr Ala Leu Val Lys His Met His Arg Ser Leu Gly Pro Pro Gln 2100 2105 2110 Gly Glu Glu Asp Ser Val Pro Arg Asp Leu Pro Ser Trp Met Lys Phe 2115 2120 2125 Leu His Gly Lys Leu Gly Asn Pro Ile Val Pro Leu Asn Ile Arg Leu 2135 2140 Phe Leu Ala Lys Leu Val Ile Asn Thr Glu Glu Val Phe Arg Pro Tyr 2145 2150 2155 Ala Lys His Trp Leu Ser Pro Leu Leu Gln Leu Ala Ala Ser Glu Asn 2165 2170 2175

Asn Gly Gly Glu Gly Ile His Tyr Met Val Val Glu Ile Val Ala Thr 2180 2185 Ile Leu Ser Trp Thr Gly Leu Ala Thr Pro Thr Gly Val Pro Lys Asp 2195 2200 Glu Val Leu Ala Asn Arg Leu Leu Asn Phe Leu Met Lys His Val Phe 2210 2215 2220 His Pro Lys Arg Ala Val Phe Arg His Asn Leu Glu Ile Ile Lys Thr 2230 2235 Leu Val Glu Cys Trp Lys Asp Cys Leu Ser Ile Pro Tyr Arg Leu Ile 2250 2245 Phe Glu Lys Phe Ser Gly Lys Asp Pro Asn Ser Lys Asp Asn Ser Val 2265 2260 2270 Gly Ile Gln Leu Leu Gly Ile Val Met Ala Asn Asp Leu Pro Pro Tyr 2280 2285 Asp Pro Gln Cys Gly Ile Gln Ser Ser Glu Tyr Phe Gln Ala Leu Val 2295 2300 Asn Asn Met Ser Phe Val Arg Tyr Lys Glu Val Tyr Ala Ala Ala Ala 2310 2315 Glu Val Leu Gly Leu Ile Leu Arg Tyr Val Met Glu Arg Lys Asn Ile 2325 2330 Leu Glu Glu Ser Leu Cys Glu Leu Val Ala Lys Gln Leu Lys Gln His 2340 2345 2350 Gln Asn Thr Met Glu Asp Lys Phe Ile Val Cys Leu Asn Lys Val Thr 2355 2360 2365 Lys Ser Phe Pro Pro Leu Ala Asp Arg Phe Met Asn Ala Val Phe Phe 2370 2375 2380 Leu Leu Pro Lys Phe His Gly Val Leu Lys Thr Leu Cys Leu Glu Val 2390 2395 Val Leu Cys Arg Val Glu Gly Met Thr Glu Leu Tyr Phe Gln Leu Lys 2405 2410 Ser Lys Asp Phe Val Gln Val Met Arg His Arg Asp Glu Arg Gln Lys 2425 Val Cys Leu Asp Ile Ile Tyr Lys Met Met Pro Lys Leu Lys Pro Val 2440 2445 Glu Leu Arg Glu Leu Leu Asn Pro Val Val Glu Phe Val Ser His Pro 2450 2455 2460 Ser Thr Thr Cys Arg Glu Gln Met Tyr Asn Ile Leu Met Trp Ile His 2470 2475 Asp Asn Tyr Arg Asp Pro Glu Ser Glu Thr Asp Asn Asp Ser Gln Glu 2485 2490 2495 Ile Phe Lys Leu Ala Lys Asp Val Leu Ile Gln Gly Leu Ile Asp Glu 2505 2510 Asn Pro Gly Leu Gln Leu Ile Ile Arg Asn Phe Trp Ser His Glu Thr 2515 2520 2525 Arg Leu Pro Ser Asn Thr Leu Asp Arg Leu Leu Ala Leu Asn Ser Leu 2535 2540 Tyr Ser Pro Lys Ile Glu Val His Phe Leu Ser Leu Ala Thr Asn Phe 2550 2555 Leu Leu Glu Met Thr Ser Met Ser Pro Asp Tyr Pro Asn Pro Met Phe 2570 2565 Glu His Pro Leu Ser Glu Cys Glu Phe Gln Glu Tyr Thr Ile Asp Ser 2585 Asp Trp Arg Phe Arg Ser Thr Val Leu Thr Pro Met Phe Val Glu Thr 2600 2605

Gln Ala Ser Gln Gly Thr Leu Gln Thr Arg Thr Gln Glu Gly Ser Leu Ser Ala Arg Trp Pro Val Ala Gly Gln Ile Arg Ala Thr Gln Gln His Asp Phe Thr Leu Thr Gln Thr Ala Asp Gly Arg Ser Ser Phe Asp Trp Leu Thr Gly Ser Ser Thr Asp Pro Leu Val Asp His Thr Ser Pro 2665 2670 Ser Ser Asp Ser Leu Leu Phe Ala His Lys Arg Ser Glu Arg Leu Gln Arg Ala Pro Leu Lys Ser Val Gly Pro Asp Phe Gly Lys Lys Arg Leu Gly Leu Pro Gly Asp Glu Val Asp Asn Lys Val Lys Gly Ala Ala Gly Arg Thr Asp Leu Leu Arg Leu Arg Arg Arg Phe Met Arg Asp Gln Glu Lys Leu Ser Leu Met Tyr Ala Arg Lys Gly Val Ala Glu Gln Lys Arg Glu Lys Glu Ile Lys Ser Glu Leu Lys Met Lys Gln Asp Ala Gln Val Val Leu Tyr Arg Ser Tyr Arg His Gly Asp Leu Pro Asp Ile Gln Ile 2775 2780 Lys His Ser Ser Leu Ile Thr Pro Leu Gln Ala Val Ala Gln Arg Asp 2790 2795 Pro Ile Ile Ala Lys Gln Leu Phe Ser Ser Leu Phe Ser Gly Ile Leu 2805 2810 2815 Lys Glu Met Asp Lys Phe Lys Thr Leu Ser Glu Lys Asn Asn Ile Thr Gln Lys Leu Leu Gln Asp Phe Asn Arg Phe Leu Asn Thr Thr Phe Ser Phe Phe Pro Pro Phe Val Ser Cys Ile Gln Asp Ile Ser Cys Gln His Ala Ala Leu Leu Ser Leu Asp Pro Ala Ala Val Ser Ala Gly Cys Leu Ala Ser Leu Gln Gln Pro Val Gly Ile Arg Leu Leu Glu Glu Ala Leu Leu Arg Leu Pro Ala Glu Leu Pro Ala Lys Arg Val Arg Gly Lys Ala Arg Leu Pro Pro Asp Val Leu Arg Trp Val Glu Leu Ala Lys Leu 2915 2920 Tyr Arg Ser Ile Gly Glu Tyr Asp Val Leu Arg Gly Ile Phe Thr Ser Glu Ile Gly Thr Lys Gln Ile Thr Gln Ser Ala Leu Leu Ala Glu Ala Arg Ser Asp Tyr Ser Glu Ala Ala Lys Gln Tyr Asp Glu Ala Leu Asn Lys Gln Asp Trp Val Asp Gly Glu Pro Thr Glu Ala Glu Lys Asp Phe Trp Glu Leu Ala Ser Leu Asp Cys Tyr Asn His Leu Ala Glu Trp Lys Ser Leu Glu Tyr Cys Ser Thr Ala Ser Ile Asp Ser Glu Asn Pro Pro Asp Leu Asn Lys Ile Trp Ser Glu Pro Phe Tyr Gln Glu Thr Tyr Leu

Pro Tyr Met Ile Arg Ser Lys Leu Lys Leu Leu Gln Gly Glu Ala Asp Gln Ser Leu Leu Thr Phe Ile Asp Lys Ala Met His Gly Glu Leu Gln Lys Ala Ile Leu Glu Leu His Tyr Ser Gln Glu Leu Ser Leu Leu Tyr Leu Leu Gln Asp Asp Val Asp Arg Ala Lys Tyr Tyr Ile Gln Asn Gly Ile Gln Ser Phe Met Gln Asn Tyr Ser Ser Ile Asp Val Leu Leu His Gln Ser Arg Leu Thr Lys Leu Gln Ser Val Gln Ala Leu Thr Glu Ile Gln Glu Phe Ile Ser Phe Ile Ser Lys Gln Gly Asn Leu Ser Ser Gln Val Pro Leu Lys Arg Leu Leu Asn Thr Trp Thr Asn Arg Tyr Pro 3160 3165 Asp Ala Lys Met Asp Pro Met Asn Ile Trp Asp Asp Ile Ile Thr Asn Arg Cys Phe Phe Leu Ser Lys Ile Glu Glu Lys Leu Thr Pro Leu Pro 3190 3195 Glu Asp Asn Ser Met Asn Val Asp Gln Asp Gly Asp Pro Ser Asp Arg 3205 3210 3215 Met Glu Val Gln Glu Glu Glu Asp Ile Ser Ser Leu Ile Arg Ser 3220 3225 Cys Lys Phe Ser Met Lys Met Lys Met Ile Asp Ser Ala Arg Lys Gln 3235 3240 Asn Asn Phe Ser Leu Ala Met Lys Leu Leu Lys Glu Leu His Lys Glu Ser Lys Thr Arg Asp Asp Trp Leu Val Ser Trp Val Gln Ser Tyr Cys Arg Leu Ser His Cys Arg Ser Arg Ser Gln Gly Cys Ser Glu Gln Val Leu Thr Val Leu Lys Thr Val Ser Leu Leu Asp Glu Asn Asn Val Ser Ser Tyr Leu Xaa Lys Asn Ile Leu Ala Phe Arg Asp Gln Asn Ile Leu Leu Gly Thr Thr Tyr Arg Ile Ile Ala Asn Ala Leu Ser Ser Glu Pro Ala Cys Leu Ala Glu Ile Glu Glu Asp Lys Ala Arg Arg Ile Leu Glu Leu Ser Gly Ser Ser Ser Glu Asp Ser Glu Lys Val Ile Ala Gly Leu Tyr Gln Arg Ala Phe Gln His Leu Ser Glu Ala Val Gln Ala Ala Glu Glu Glu Ala Gln Pro Pro Ser Trp Ser Cys Gly Pro Ala Ala Gly Val Ile Asp Ala Tyr Met Thr Leu Ala Asp Phe Cys Asp Gln Gln Leu Arg Lys Glu Glu Glu Asn Ala Ser Val Thr Asp Ser Ala Glu Leu Gln Ala Tyr Pro Ala Leu Val Val Glu Lys Met Leu Lys Ala Leu Lys Leu Asn Ser Asn Glu Ala Arg Leu Lys Phe Pro Arg Leu Leu Gln Ile Ile Glu

Arg Tyr Pro Glu Glu Thr Leu Ser Leu Met Thr Lys Glu Ile Ser Ser 3475 3480 Val Pro Cys Trp Gln Phe Ile Ser Trp Ile Ser His Met Val Ala Leu 3495 3500 Leu Asp Lys Asp Gln Ala Val Ala Val Gln His Ser Val Glu Glu Ile 3510 3515 Thr Asp Asn Tyr Pro Gln Ala Ile Val Tyr Pro Phe Ile Ile Ser Ser 3525 3530 Glu Ser Tyr Ser Phe Lys Asp Thr Ser Thr Gly His Lys Asn Lys Glu 3540 3545 3550 Phe Val Ala Arg Ile Lys Ser Lys Leu Asp Gln Gly Val Ile Gln 3555 3560 3565 Asp Phe Ile Asn Ala Leu Asp Gln Leu Ser Asn Pro Glu Leu Leu Phe 3575 3580 Lys Asp Trp Ser Asn Asp Val Arg Ala Glu Leu Ala Lys Thr Pro Val 3590 3595 Asn Lys Lys Asn Ile Glu Lys Met Tyr Glu Arg Met Tyr Ala Ala Leu 3605 3610 3615 Gly Asp Pro Lys Ala Pro Gly Leu Gly Ala Phe Arg Arg Lys Phe Ile 3625 3630 Gln Thr Phe Gly Lys Glu Phe Asp Lys His Phe Gly Lys Gly Gly Ser 3635 3640 3645 Lys Leu Leu Arg Met Lys Leu Ser Asp Phe Asn Asp Ile Thr Asn Met 3650 3655 3660 Leu Leu Lys Met Asn Lys Asp Ser Lys Pro Pro Gly Asn Leu Lys 3665 3670 3675 Glu Cys Ser Pro Trp Met Ser Asp Phe Lys Val Glu Phe Leu Arg Asn 3685 3690 3695 Glu Leu Glu Ile Pro Gly Gln Tyr Asp Gly Arg Gly Lys Pro Leu Pro 3700 3705 3710 Glu Tyr His Val Arg Ile Ala Gly Phe Asp Glu Arg Val Thr Val Met 3720 3725 Ala Ser Leu Arg Arg Pro Lys Arg Ile Ile Ile Arg Gly His Asp Glu 3735 3740 Arg Glu His Pro Phe Leu Val Lys Gly Gly Glu Asp Leu Arg Gln Asp 3750 3755 Gln Arg Val Glu Gln Leu Phe Gln Val Met Asn Gly Ile Leu Ala Gln 3765 3770 3775 Asp Ser Ala Cys Ser Gln Arg Ala Leu Gln Leu Arg Thr Tyr Ser Val 3780 3785 3790 Val Pro Met Thr Ser Ser Asp Pro Arg Ala Pro Pro Cys Glu Tyr Lys 3795 3800 3805 Asp Trp Leu Thr Lys Met Ser Gly Lys His Asp Val Gly Ala Tyr Met 3815 3820 Leu Met Tyr Lys Gly Ala Asn Arg Thr Glu Thr Val Thr Ser Glu Arg 3830 3835 Lys Arg Glu Ser Lys Val Pro Ala Asp Leu Leu Lys Arg Ala Phe Val 3845 3850 Arg Met Ser Thr Ser Pro Glu Ala Phe Leu Ala Leu Arg Ser His Phe 3865 3860 3870 Ala Ser Ser His Ala Leu Ile Cys Ile Ser His Trp Ile Leu Gly Ile 3880 Gly Asp Arg His Leu Asn Asn Phe Met Val Ala Met Glu Thr Gly Gly 3895 3900

Val Ile Gly Ile Asp Phe Gly His Ala Phe Gly Ser Ala Thr Gln Phe 3910 3915 Leu Pro Val Pro Glu Leu Met Pro Phe Arg Leu Thr Arg Gln Phe Ile 3925 3930 Asn Leu Met Leu Pro Met Lys Glu Thr Gly Leu Met Tyr Ser Ile Met 3945 3940 Val His Ala Leu Arg Ala Phe Arg Ser Asp Pro Gly Leu Leu Thr Asn 3965 3960 Thr Met Asp Val Phe Val Lys Glu Pro Ser Phe Asp Trp Lys Asn Phe 3970 3975 3980 Glu Gln Lys Met Leu Lys Lys Gly Gly Ser Trp Ile Gln Glu Ile Asn 3990 3995 Val Ala Glu Lys Asn Trp Tyr Pro Arg Gln Lys Ile Cys Tyr Ala Lys 4005 4010 Arg Lys Leu Ala Gly Ala Asn Pro Ala Val Ile Thr Cys Asp Glu Leu 4025 4020 Leu Leu Gly His Glu Lys Ala Pro Ala Phe Arg Asp Tyr Val Ala Val 4040 4045 Ala Arg Gly Ser Lys Asp His Asn Ile Arg Ala Gln Glu Pro Glu Ser 4050 4055 4060 Gly Leu Ser Glu Glu Thr Gln Val Lys Cys Ile Met Asp Gln Ala Thr 4065 4070 4075 Asp Pro Asn Ile Leu Gly Arg Thr Trp Glu Gly Trp Glu Pro Trp Met 4085 4090

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Gly Cys Phe Val Lys Asn Arg Glu Glu Leu Gly Phe Arg Pro Glu Tyr Ser Ala Ser Gln Leu Lys Gly Phe Ser Leu Leu Ala Thr Glu Asp Lys Glu Ala Leu Lys Lys Gln Leu Pro Gly Val Lys Ser Glu Gly Lys Arg Lys Gly Asp Glu Val Asp Gly Val Asp Glu Val Ala Lys Lys Lys Ser Lys Lys Glu Lys Asp Lys Asp Ser Lys Leu Glu Lys Ala Leu Lys Ala Gln Asn Asp Leu Ile Trp Asn Ile Lys Asp Glu Leu Lys Lys Val Cys Ser Thr Asn Asp Leu Lys Glu Leu Leu Ile Phe Asn Lys Gln Gln Val Pro Ser Gly Glu Ser Ala Ile Leu Asp Arg Val Ala Asp Gly Met Val Phe Gly Ala Leu Leu Pro Cys Glu Glu Cys Ser Gly Gln Leu Val Phe Lys Ser Asp Ala Tyr Tyr Cys Thr Gly Asp Val Thr Ala Trp Thr Lys Cys Met Val Lys Thr Gln Thr Pro Asn Arg Lys Glu Trp Val Thr Pro Lys Glu Phe Arg Glu Ile Ser Tyr Leu Lys Lys Leu Lys Val Lys Lys Gln Asp Arg Ile Phe Pro Pro Glu Thr Ser Ala Ser Val Ala Ala Thr Pro Pro Pro Ser Thr Ala Ser Ala Pro Ala Ala Val Asn Ser Ser Ala Ser Ala Asp Lys Pro Leu Ser Asn Met Lys Ile Leu Thr Leu Gly Lys Leu Ser Arg Asn Lys Asp Glu Val Lys Ala Met Ile Glu Lys Leu Gly Gly Lys Leu Thr Gly Thr Ala Asn Lys Ala Ser Leu Cys Ile Ser Thr Lys Lys Glu Val Glu Lys Met Asn Lys Lys Met Glu Glu Val Lys Glu Ala Asn Ile Arg Val Val Ser Glu Asp Phe Leu Gln Asp Val Ser Ala Ser Thr Lys Ser Leu Gln Glu Leu Phe Leu Ala His Ile Leu Ser Pro Trp Gly Ala Glu Val Lys Ala Glu Pro Val Glu Val Val Ala Pro Arg Gly Lys Ser Gly Ala Ala Leu Ser Lys Lys Ser Lys Gly Gln Val Lys Glu Glu Gly Ile Asn Lys Ser Glu Lys Arg Met Lys Leu Thr Leu Lys Gly Gly Ala Ala Val Asp Pro Asp Ser Gly Leu Glu His Ser Ala His Val Leu Glu Lys Gly Gly Lys Val Phe Ser Ala Thr Leu Gly Leu Val Asp Ile Val Lys Gly Thr Asn Ser Tyr Tyr Lys Leu Gln Leu Leu Glu Asp Asp Lys Glu Asn Arg Tyr Trp Ile Phe Arg Ser Trp Gly Arg Val

Gly Thr Val Ile Gly Ser Asn Lys Leu Glu Gln Met Pro Ser Lys Glu Asp Ala Ile Glu His Phe Met Lys Leu Tyr Glu Glu Lys Thr Gly Asn Ala Trp His Ser Lys Asn Phe Thr Lys Tyr Pro Lys Lys Phe Tyr Pro Leu Glu Ile Asp Tyr Gly Gln Asp Glu Glu Ala Val Lys Lys Leu Thr Val Asn Pro Gly Thr Lys Ser Lys Leu Pro Lys Pro Val Gln Asp Leu Ile Lys Met Ile Phe Asp Val Glu Ser Met Lys Lys Ala Met Val Glu Tyr Glu Ile Asp Leu Gln Lys Met Pro Leu Gly Lys Leu Ser Lys Arg Gln Ile Gln Ala Ala Tyr Ser Ile Leu Ser Glu Val Gln Gln Ala Val Ser Gln Gly Ser Ser Asp Ser Gln Ile Leu Asp Leu Ser Asn Arg Phe Tyr Thr Leu Ile Pro His Asp Phe Gly Met Lys Lys Pro Pro Leu Leu Asn Asn Ala Asp Ser Val Gln Ala Lys Val Glu Met Leu Asp Asn Leu Leu Asp Ile Glu Val Ala Tyr Ser Leu Leu Arg Gly Gly Ser Asp Asp Ser Ser Lys Asp Pro Ile Asp Val Asn Tyr Glu Lys Leu Lys Thr Asp Ile Lys Val Val Asp Arg Asp Ser Glu Glu Ala Glu Ile Ile Arg Lys Tyr Val Lys Asn Thr His Ala Thr Thr His Asn Ala Tyr Asp Leu Glu Val Ile Asp Ile Phe Lys Ile Glu Arg Glu Gly Glu Cys Gln Arg Tyr Lys Pro Phe Lys Gln Leu His Asn Arg Arg Leu Leu Trp His Gly Ser Arg Thr Thr Asn Phe Ala Gly Ile Leu Ser Gln Gly Leu Arg Ile Ala Pro Pro Glu Ala Pro Val Thr Gly Tyr Met Phe Gly Lys Gly Ile Tyr Phe Ala Asp Met Val Ser Lys Ser Ala Asn Tyr Cys His Thr Ser Gln Gly Asp Pro Ile Gly Leu Ile Leu Leu Gly Glu Val Ala Leu Gly Asn Met Tyr Glu Leu Lys His Ala Ser His Ile Ser Lys Leu Pro Lys Gly Lys His Ser Val Lys Gly Leu Gly Lys Thr Thr Pro Asp Pro Ser Ala Asn Ile Ser Leu Asp Gly Val Asp Val Pro Leu Gly Thr Gly Ile Ser Ser Gly Val Asn Asp Thr Ser Leu Leu Tyr Asn Glu Tyr Ile Val Tyr Asp Ile Ala Gln Val Asn Leu Lys Tyr Leu Leu Lys Leu Lys Phe Asn Phe Lys Thr Ser Leu Trp

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